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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,622	02/07/2002	Lieping Chen	07039-331001	3225

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,622	CHEN ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 12-27* is/are pending in the application.

4a) Of the above claim(s) *8 and 12-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment/remarks, filed 10/06/2005, are acknowledged.

Claims 2 and 9 – 11 have been cancelled.

Claims 1, 3 – 7, and 12 – 17 have been amended.

Claims 24 – 27 have been added.

Claims 1, 3 – 8, and 12 – 27 are pending.

Claims 8 and 12 – 23 have been withdrawn from consideration by the Examiner as being drawn to nonelected inventions.

Claims 1, 3 – 7, and 24 – 27 are under consideration.

Applicant is reminded that the proper claim status identifier for claims 12 – 17 is "withdrawn – currently amended." See MPEP §714(c)(2).

2. This Office Action will be in response to applicant's arguments, filed 10/06/2005.

The rejections of record can be found in the previous Office Action, mailed 05/03/2005.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

It is noted that New Grounds of Rejection are set forth herein.

3. The objections and rejections of record have been withdrawn in view of Applicant's amendment and arguments, except as set forth herein.

4. Claims 1 and 3 – 7 stand rejected, and newly added claims 24 – 27 are rejected, under **35 U.S.C. 112, second paragraph,** as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The claims are indefinite in the recitation of "B7-H2" because its identity is unclear.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that the specification makes it clear that human and mouse "B7-H2" polypeptides are covered by the term.

This is not found persuasive, because, while the specification mentions that human and mouse polypeptides are covered by the term "B7-H2," the specification does not sufficiently define the metes and bounds of the invention (i.e. are the polypeptides of other species encompassed within the scope of the claims?). Furthermore, as noted previously, the name "B7-H2" is also used to designate a different B7-related protein (e.g. Coyle et al., US Patent No. 6,630,575; see e.g. Summary of Invention at columns 3 – 4). Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

Amending the claims to recite the appropriate SEQ ID Number would obviate this rejection.

B. Claims 3 – 6 are indefinite as being dependent on cancelled claims.

It is suggested that applicant rewrite the claims in independent form to include the limitations of base claims. Alternatively, the claims may be amended to depend on other base claims currently under consideration.

It appears that claims 3 and 5 were intended to depend on claim 1, which dependence is assumed herein for examination purposes.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

5. Claims 1, 3 – 7, and 24 – 27 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a New Matter rejection.*

A. Applicant's amendment asserts that no New Matter has been added and points to the specification at pages 3, 5, 7, 8, and 11 for support for the newly added limitations of claim 1. However, the specification does not appear to provide an adequate written description of a "variant consisting of an amino acid sequence that **differs by one or more amino acid substitutions** from [ ] its corresponding wild-type ICOS amino acid sequence."

B. Applicant's amendment asserts that no New Matter has been added and points to the specification at pages 8, 11, and 18 for support for the newly added claim 26. However, the specification does not appear to provide an adequate written description of a fusion polypeptide comprising ICOS and an "**immunoglobulin Fc fragment** sequence." It is noted that the specification mentions ICOS-Ig polypeptide (page 11 lines 27 – 29), and an ICOS-Ig polypeptide produced by fusing the extracellular domain of human ICOS to the "CH2-CH3 portion of human IgG1." However, this is not seen as providing sufficient support under 35 USC 112, first paragraph, for the generic recitation of "immunoglobulin Fc fragment."

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the New Matter in the response to this Office Action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

6. Claims 1 – 3, 5, and 7 stand rejected, and newly added claims 24 – 27 are rejected, under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a polypeptide which differs from SEQ ID NO:12 by the specific amino acid substitutions recited in claims 4 and 6, does not reasonably provide enablement for the broadly recited genus of including polypeptides at least 75% homologous to wild-type ICOS, and polypeptides comprising fragments of at least 8 amino acids of the extracellular domain of ICOS.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that in view of the teachings of the instant specification regarding the critical residues of ICOS, and the high level of knowledge of those skilled in the art, the experimentation necessary to identify the polypeptide variants and fragments having the requisite function would be of a routine nature.

This is not found persuasive, because the skilled artisan, upon reviewing the instant disclosure, in particular Table 3 at page 26, an in view of knowledge in the art, would have concluded that a great majority of amino acid substitutions in ICOS would result in completely abolished ligand binding (denoted as B7-H2 binding activity of less that 0.1% of wild type in Table 3). Therefore, given the enormous number of variants and fragments encompassed by the instant claims language, and the fact that only a small proportion of those are expected to possess the requisite functional properties, the experimentation left to those skilled in the art, remains unnecessarily, and improperly, extensive and undue.

Applicant further argues that by amending claim 1 the range of polypeptide covered by the claims is greatly reduced.

This is not found persuasive, because introducing the limitation of 75% identity into the claims does not change their scope, because the original recitation of "substantial homology" has been interpreted in light of the specification to mean 75% identity, as noted in the prior Office Action. Furthermore, limiting the plethora of variants

to those corresponding to the extracellular domain of ICOS only insignificantly reduces the number of possibilities the skilled artisan would be required to analyze, because the extracellular domain constitutes more than half of the ICOS polypeptide (e.g. SEQ ID NOS: 10 and 12).

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

7. Claims 1 and 7 stand rejected, and newly added claims 24 – 26 are rejected under **35 U.S.C. 102(e)** as being anticipated by Tamatani et al. (US Pat. Pub. 2002/0156242).

Applicant's arguments have been fully considered but have not been found convincing.

Applicant argues that the instant claim 1 requires that the variant ICOS polypeptide or portion thereof contain one or more amino acid substitutions, while no specific substitutions are mentioned by Tamatani et al. In response, no specific substitutions are mentioned in the instant claim 1 either. Tamatani et al. teach polypeptides having 60% or more homology to wild-type ICOS (e.g. paragraph 0056), which thus contain one or more amino acid substitutions.

Applicant further argues that the instant claim 1 requires that the claimed ICOS variant have altered affinity for B7-H2, and that it in not necessarily the case that amino acid variants mentioned by Tamatani et al. would have resulted in altered affinity to B7-H2.

This is not found persuasive, because Tamatani et al. teach e.g. at paragraph 0159 that following the introduction of amino acid substitutions into ICOS, the resulting variant polypeptides should be screened for biological activity to identify mutants that retain activity. Inherent in this teaching is the recognition that the remaining mutants would not have retained biological activity, i.e. would have altered activity. Since binding to its ligand is the principal biological activity of ICOS, sequence variants of ICOS with altered biological activity are inherent in the teachings of Tamatani et al.

The newly added claims 24 – 26 are included in the rejection, because Tamatani et al. teach fusion polypeptides comprising ICOS variants and a human Ig heavy chain or portion of the constant region (e.g. paragraph 0072).

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

8. Conclusion: no claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

November 29, 2005

PHILLIP GAMBEL, PH.D
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11/29/05